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Predictors of Complications After Percutaneous Gallbladder Drainage in Acute Cholecystitis: The Role of Direct Bilirubin and Bile Culture Positivity

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Abstract

Background Acute cholecystitis (AC) is a potentially severe inflammatory condition of the gallbladder, most commonly caused by gallstone obstruction. In high-risk patients, percutaneous gallbladder drainage (PGD) is widely used as a bridge or alternative to surgery. However, predictors of post-PGD complications remain insufficiently defined. This study aimed to investigate the prognostic value of direct bilirubin levels and bile culture positivity in predicting complications following PGD.

Methods We conducted a retrospective cohort study including patients with Grade II and III AC, according to the Tokyo Guidelines 2018, who underwent PGD between 2015 and 2024. Patients with acalculous cholecystitis, biliary strictures, or malignancy were excluded. Clinical, biochemical, microbiological, and radiological data were analyzed. Complications were classified using the Clavien–Dindo system. Univariate and multivariate analyses were performed to identify independent predictors of complications.

Results A total of 252 patients were included (median age: 68.5 years). Bile culture positivity was observed in 49.2% of cases, with Escherichia coli, Enterococcus spp., and Klebsiella spp. being the most frequently isolated organisms. Complications occurred more frequently in patients with diabetes mellitus (p=0.024) and positive bile cultures (p=0.007). Patients with complications demonstrated significantly elevated levels of direct bilirubin (p=0.008), total bilirubin (p=0.027), GGT (p=0.002), AST (p=0.013), and ALT (p=0.001), as well as prolonged hospital stay (p<0.001). In multivariate analysis, direct bilirubin emerged as the sole independent predictor of complications (OR=1.69, p=0.002). In surgically managed patients, complications were associated with increased rates of conversion and open cholecystectomy and a reduced rate of laparoscopic procedures.

Conclusions PGD represents an effective therapeutic strategy in high-risk AC patients; however, complication risk remains substantial. Elevated direct bilirubin is a robust independent predictor of adverse outcomes, while diabetes mellitus and bile culture positivity further contribute to risk stratification. Integration of biochemical and microbiological parameters into clinical decision-making may enhance patient selection and optimize outcomes. Prospective, large-scale studies are warranted to validate these findings.

INTRODUCTION

Acute cholecystitis (AC) is an inflammatory condition characterized by abdominal pain resulting from inflammation of the gallbladder. In approximately 90–95% of cases, the underlying cause is gallstones [1]. Obstruction of the cystic duct by gallstones leads to edema and bacterial proliferation within the bile. Delayed diagnosis or inadequate treatment may result in serious complications such as perforation, biliary peritonitis, and sepsis [2].

The treatment strategy is determined by several factors, including the severity and duration of cholecystitis, patient comorbidities, advanced age, and the surgeon’s experience. In patients with low

surgical risk, laparoscopic cholecystectomy (LC) is the first-line treatment for uncomplicated AC [3]. However, the rate of surgical complications in cholecystectomies performed for AC is higher than in elective cholecystectomies [4].

For high-risk surgical patients or those with complicated AC, percutaneous gallbladder drainage (PGD) has emerged as an effective treatment option. The 2018 Tokyo Guidelines recommend PGD in Grade II and III AC patients, particularly in experienced centers [5]. Although PGD is associated with catheter-related complications such as pain, infection, bile leakage, and catheter obstruction, it remains a viable conservative treatment modality. In addition, bile culture analysis and antimicrobial susceptibility testing allow for the administration of targeted antibiotic therapy [6–7]. Previous studies have compared appropriate antibiotic therapy with surgical intervention in elderly patients [8].

In this retrospective study, we analyzed bile culture results in patients diagnosed with AC in the emergency department who underwent PGD. We also evaluated complications in patients managed conservatively without surgery after PGD and those who subsequently underwent surgery. We believe that our findings may contribute to the development of treatment strategies based on culture results.

MATERIALS AND METHODS

This study was conducted retrospectively at the Health Sciences University Haydarpaşa Numune Training and Research Hospital. Patients admitted to the general surgery clinic with a diagnosis of acute cholecystitis (AC) in the emergency department between 2015 and 2024 were examined.

Patients who underwent percutaneous gallbladder drainage (PGD) were assessed in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist.

The diagnosis of AC was established based on the Tokyo Guidelines 2018 (TG18) diagnostic criteria. Patients with Grade II and Grade III AC according to TG18 were included in the study. In our study, patients with acute acalculous cholecystitis, biliary tract stricture, or a history of cancer were excluded.

Collected data included patient demographics (age and comorbidities), biochemical parameters at initial admission prior to PGD (white blood cell count, C-reactive protein [CRP], albumin, direct bilirubin, total bilirubin, alanine aminotransferase [ALT], aspartate aminotransferase [AST], gamma-glutamyl transferase [GGT], and alkaline phosphatase [ALP]), and radiological findings such as gallbladder diameter measured by ultrasonography or computed tomography. In addition, treatment strategy (follow-up with PGD or early cholecystectomy), bile culture results obtained during PGD, length of hospital stay, and complications classified according to the Clavien–Dindo classification were recorded and managed using Microsoft Excel.

PGD was performed by a single experienced interventional radiologist. An 8-F pigtail drainage catheter (Flexima, Boston Scientific, USA) was inserted into the gallbladder using the Seldinger technique and left in place for free drainage.

Length of hospital stay was defined as the duration from admission to the general surgery ward from the emergency department until discharge.

Bile samples were obtained via PGD under aseptic conditions. Culture results were evaluated according to the criteria of the European Committee on Antimicrobial Susceptibility Testing (EUCAST), as adopted by the Turkish Society of Microbiology.

Statistical Analysis:

Data were analyzed using R statistical software (version 4.5.2). Descriptive statistics were presented as frequency (n), percentage (%), mean ± standard deviation (mean ± SD), and median (Q1–Q3). Pearson's chi-square test was used for the comparison of categorical variables; Fisher's exact test was applied when expected cell counts were insufficient. The distribution of continuous variables was assessed using the Shapiro–Wilk normality test and Q–Q plots. Since continuous variables did not follow a normal distribution, the Mann–Whitney U test was used for group comparisons. A logistic regression model was constructed to identify independent risk factors. A p-value of < 0.05 was considered statistically significant.

RESULTS

A total of 358 patients who underwent percutaneous gallbladder drainage (PGD) between 2015 and 2024 were retrospectively reviewed. Among these, 252 patients diagnosed with acute cholecystitis (AC) in the emergency department, admitted to the general surgery clinic, and confirmed to have gallstones were included in the study. Bile culture results were available for all included patients.

Of the patients, 54.37% (n = 137) were male and 45.63% (n = 115) were female. The median age was 68.50 years (IQR: 57.50–78.00), and the median length of hospital stay was 7 days (IQR: 5–10). The most common comorbidity was diabetes mellitus (42.86%), followed by hypertension (41.43%). Coronary artery disease was present in 20.24% of patients, asthma/COPD in 7.54%, chronic kidney disease in 4.37%, and heart failure in 2.78%.

Laboratory parameters at admission showed a median WBC count of 12,645/μL, CRP of 50 mg/L, albumin of 3.6 g/L, total bilirubin of 0.88 mg/dL (0.50–1.41), direct bilirubin of 0.46 mg/dL (0.22–0.76), ALP of 92.00 U/L (66.00–123.50), GGT of 50.50 U/L (26.00–110.50), AST of 25.00 U/L (16.00–48.50), and ALT of 23.50 U/L (15.00–45.50). According to the American Society of Anesthesiologists (ASA) classification, 28 patients were ASA I, 82 were ASA II, 101 were ASA III, and 41 were ASA IV. Based on TG18 criteria, 193 patients had Grade II AC and 59 had Grade III AC.

Radiological evaluation of gallbladder diameter was performed using ultrasonography (USG) and computed tomography (CT) in 219 patients, with a median diameter of 46.00 mm (41.00–55.00). Demographic characteristics, biochemical findings, and other relevant variables are presented in Table 1.

Bile culture results demonstrated microbial growth in 124 patients (49.21%). The most frequently isolated pathogen was Escherichia coli (17.46%), followed by Enterococcus spp. (11.51%) and Klebsiella spp. (8.33%). The distribution of bacterial species is presented in Grafic 1.
Grafic 1. Distribution of Bacteria Isolated from Bile Culture (N = 252)

According to the Clavien–Dindo classification, among patients with positive bile cultures, complications were classified as Grade 0 in 80 patients, Grade I in 3 patients, Grade IIIa in 30 patients, Grade IIIb in 5 patients, Grade IV in 2 patients, and Grade V in 4 patients. Among patients without microbial growth (n = 128, 50.79%), complications were classified as Grade 0 in 104 patients, Grade II in 1 patient, Grade IIIa in 18 patients, Grade IIIb in 1 patient, Grade IV in 3 patients, and Grade V in 1 patient (Table 2).

Table 2
Number of complications in patients who underwent surgery and those who did not, with and without bacterial growth in culture, according to the Clavian Dindo Classification.

Clavian Dindo Grade	**Surgery performed (n:121)**	**Non-surgical (n:131)**	**Bacterial culture + (n:124)**	**bacterial culture – (n:128)**
0	90	95	80	104
1	2	1	3	0
2	0	1	0	1
3a	22	26	30	18
3b	6	0	5	1
4	1	4	2	3
5	0	4	4	1

After removal of the PGD catheter, elective cholecystectomy was planned in 121 patients (40.02%) at an interval of approximately 6–8 weeks. Surgical procedures included laparoscopic cholecystectomy (LC) in 85 patients (33.73%), conversion cholecystectomy in 18 patients (7.14%), open cholecystectomy in 10 patients (3.97%), partial cholecystectomy in 6 patients (2.38%), and cholecystectomy with choledochoduodenostomy in 2 patients (0.79%).

In surgically treated patients, complications according to the Clavien–Dindo classification were Grade 0 in 90 patients, Grade I in 2 patients, Grade IIIa in 22 patients, Grade IIIb in 6 patients, and Grade IV in 1 patient (Table 2).

When surgical approaches were compared between patients with and without PGD-related complications, conversion cholecystectomy was more frequent in patients with complications (11.76% vs. 5.43%), as was open cholecystectomy (7.35% vs. 2.72%). In contrast, laparoscopic cholecystectomy was less frequently performed in patients with complications (20.59% vs. 38.59%).

A total of 131 patients (51.98%) who did not undergo surgery after PGD were retrospectively analyzed. Complications occurring during catheter insertion, follow-up, and after catheter removal were evaluated. According to the Clavien–Dindo classification, 95 patients were Grade 0, 1 patient Grade I, 1 patient Grade II, 26 patients Grade IIIa, 4 patients Grade IV, and 4 patients Grade V (Table 2).

Follow-up data were available for 58 patients in whom surgery was not planned after catheter removal. These patients were followed for a median of 11.50 months (6.00–24.00). Radiological evaluation (USG, CT, MRCP) revealed a normal gallbladder in 24 patients (41.38%), contracted gallbladder in 21 patients (36.21%), recurrent AC in 3 patients (5.17%), and mechanical jaundice requiring ERCP due to choledocholithiasis in 10 patients (17.24%).

In the overall cohort of patients undergoing PGD for AC, diabetes mellitus ($p = 0.024$) and positive bile culture ($p = 0.007$) were identified as significant risk factors for complications. No significant differences were observed between groups in terms of gender, hypertension, coronary artery disease, asthma/COPD, heart failure, or chronic kidney disease.

Among laboratory parameters, direct bilirubin ($p = 0.008$), total bilirubin ($p = 0.027$), GGT ($p = 0.002$), AST ($p = 0.013$), and ALT ($p = 0.001$) levels were significantly higher in patients who developed complications. Length of hospital stay was also significantly longer in the complication group ($p < 0.001$). No statistically significant differences were found between groups in terms of age, gallbladder diameter, WBC, CRP, or albumin levels ($p > 0.05$). Comparative analyses of continuous and categorical variables are presented in Tables 3 and 4.

Table 3
Comparison of Continuous Variables by Complication — Median (Q1–Q3)

Variable	n	No complications (n:184)	Complications (n:68)	p
Age (years)	252	68.00 (57.00–77.00)	69.50 (60.50–80.50)	0.309
Gallbladder diameter (mm)	219	46.00 (40.00–55.00)	47.50 (41.00–55.00)	0.780
WBC (×10³/μL)	252	13090 (9095–16710)	10840 (8950–15705)	0.259
CRP (mg/L)	252	56.83 (12.50–172.00)	46.99 (16.50–183.16)	0.728
Albumin (g/L)	252	36.80 (31.75–40.13)	35.00 (30.00–39.50)	0.265
Direct Bilirubin (mg/dL)	252	0.38 (0.22–0.70)	0.58 (0.26–1.01)	**0.008***
Total Bilirubin (mg/dL)	252	0.76 (0.49–1.33)	1.17 (0.61–1.97)	**0.027***
ALP (U/L)	252	88.00 (65.50–116.00)	101.00 (69.50–168.50)	0.076
GGT (U/L)	252	42.00 (23.00–104.00)	72.00 (42.00–135.00)	**0.002***
AST (U/L)	252	23.00 (16.00–41.50)	29.00 (19.50–57.00)	**0.013***
ALT (U/L)	252	21.00 (14.00–42.50)	32.50 (20.00–57.50)	**0.001***
Hospital stay duration (days)	252	6.00 (5.00–8.00)	8.50 (5.00–14.00)	**< 0.001***
Tracking Time (days)	58	10.00 (6.00–24.00)	19.50 (7.50–30.50)	0.212

* $p < 0.05$ is statistically significant (rows highlighted in yellow)

Table 4
Comparison of Categorical Variables by Complication

Variable	No complications (n:184)	Complications (n:68)	p
Gender (Male)	103 (55.98%)	34 (50.00%)	0.398
Diabetes (Yes)	71 (38.59%)	37 (54.41%)	**0.024***
Hypertension (Yes)	79 (42.93%)	25 (36.76%)	0.209
Coronary Artery Disease (Yes)	34 (18.48%)	17 (25.00%)	0.253
Asthma/COPD (Yes)	15 (8.15%)	4 (5.88%)	0.545
Heart Failure (Yes)	6 (3.26%)	1 (1.47%)	0.678
Chronic Renal Failure (Yes)	8 (4.35%)	3 (4.41%)	1.000
Growth in Bile Culture (Present)	81 (44.02%)	43 (63.24%)	**0.007***

* p<0.05 is statistically significant (rows highlighted in yellow)

The distribution of bacterial species differed significantly between complication groups (chi-square test, p = 0.016). The rate of positive cultures was higher in patients with complications (63.24% vs. 44.02%). In particular, Klebsiella spp. (14.71% vs. 5.98%) and Enterococcus spp. (17.65% vs. 9.24%) were more frequently isolated in the complication group. However, in post-hoc analysis with Bonferroni correction (critical z = 2.955, number of cells = 16), no individual cell reached statistical significance.

DISCUSSION

In this study, we retrospectively analyzed the outcomes of PGD performed in 252 patients. We evaluated complications in patients who underwent elective surgery after PGD as well as those who were managed conservatively without surgery.

As highlighted in the CHOCOLATE trial published in 2018, age and the presence of comorbidities are important risk factors for complications when determining the optimal treatment strategy in patients diagnosed with acute cholecystitis (AC) [9]. In our study, the median age of the study population was 68.50 years, with a slight predominance of male patients (54.37%). However, advanced age alone was not identified as a risk factor for increased PGD-related complications. Advanced age by itself should not be considered an absolute indication for PGD. Rather, the presence of comorbidities and higher ASA scores in elderly patients constitute the main indications for PGD, which can be considered a bridging treatment modality [10–12].

Among comorbid conditions, diabetes mellitus was found to significantly increase the rate of complications, with a prevalence of 42.86% in our study. Hypertension was present in 41.43% of patients but was not identified as a significant risk factor for complications. Numerous studies in the literature have reported the association between diabetes mellitus and increased complication rates in AC [13–14]. Although diabetes alone is not considered an absolute risk factor for PGD-related complications, it may contribute to an increased risk in elderly patients and those with severe cholecystitis [15–16].

In patients who developed complications, direct bilirubin, total bilirubin, and cholestatic parameters (GGT, AST, ALT), as well as length of hospital stay, were significantly higher. In multivariate analysis, direct bilirubin level was identified as the only independent risk factor for the development of complications (OR = 1.69, p = 0.002). Previous studies investigating this issue have similarly reported that elevated direct bilirubin levels may be useful in predicting complications and are associated with prolonged hospitalization [17–19].

The complication rate was significantly higher in patients with bacterial growth in bile culture. The most frequently isolated bacteria were Escherichia coli, Enterococcus, and Klebsiella. The distribution of bacterial types showed statistically significant differences among the complication groups (Chi-square test, p = 0.016), however, no individually significant bacteria were found in the Bonferroni corrected post-

hoc analysis (critical z = 2.955, cell count = 16). Although there are not many studies on bile culture in AC in the literature, the bacteria growing in bile culture in the study by Lahav et al. in 2025 and the bacteria growing in our study in the article published in the Journal of Vascular and Interventional Radiology in 2012 are consistent [20–21]. There are studies indicating that the presence of bacterial growth in bile culture increases complications. A large cohort study by Ramírez-Giraldo C et al. showed that patients with positive bile cultures had more severe disease and more complications [22].

In patients who underwent surgery, a significant association was observed between complications and positive bile culture results. However, although the odds ratios were relatively high for Enterococcus growth (OR = 2.49, p = 0.062), conversion to open surgery (OR = 2.94, p = 0.053), and primary open surgery (OR = 3.45, p = 0.091), these variables did not reach statistical significance.

In patients who underwent cholecystectomy combined with choledochoduodenostomy, the extremely high odds ratio (OR = 12,126,432.41) and infinite confidence interval were attributed to the very small sample size in this subgroup (n = 2) and were therefore not considered clinically meaningful.

There are limited studies in the literature evaluating the relationship between bile culture results and postoperative complications in patients undergoing cholecystectomy after PGD. In a study by Yoon JH et al., no significant association was found between bile culture positivity and increased complication rates in patients undergoing cholecystectomy for acute cholecystitis [23]. Similarly, a study published in 2022 reported no correlation between bile culture results and surgical site infections or postoperative complications [24].

In contrast, an analysis conducted at Dr. José Eleuterio González University Hospital on patients undergoing laparoscopic cholecystectomy demonstrated that all patients who developed surgical site infections had positive bacterial growth in bile cultures [25]. Additionally, there are studies suggesting that appropriate antibiotic therapy in patients with positive bile cultures may reduce surgical complications [26].

Although bile culture positivity may indicate a more severe clinical course in acute cholecystitis, further studies are needed to establish whether it can be considered an independent risk factor for PGD-related or surgical complications.

Bile culture analysis in patients undergoing PGD does not impose additional comorbidity or require further invasive procedures. Therefore, we suggest that tailoring antibiotic therapy based on bile culture results may reduce both PGD-related complications in conservatively managed patients and postoperative complications in those undergoing surgery.

CONCLUSION

PGD is a bridging method in AC patients. However, it can cause some complications. In AC patients who have and have not undergone surgery, it has been shown that elevated cholestasis parameters can be a

warning sign for the development of complications, and direct bilirubin levels are an independent predictor. Diabetes and a positive bile culture are also among the factors that increase the risk of complications. Large-scale studies are needed to determine whether bile culture evaluations can be considered a criterion for predicting complications in patients undergoing PGD.

Declarations

Funding:

This research received no external funding.

Conflict of Interest:

The authors declare no conflict of interest.

Ethical Approval:

Ethical approval was obtained from the Ethics Committee of Haydarpaşa Numune Training and Research Hospital (Approval No: [HNEAH-GOAEK 2026/20]). The study was conducted in accordance with the Helsinki Declaration.

Author Contributions:

Concept: F.C.; Design: F.C.; Data Collection: D.B., E.B.A., R.B.; Analysis: F.C., K.Ç.; Writing: F.C., M.O.G.; Supervision: F.C.

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Consent to Participate: Informed consent was obtained from each patient upon admission to the hospital.

Clinical Trial Number: not applicable

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Table 1

Table 1 is available in the Supplementary Files section.

Figures

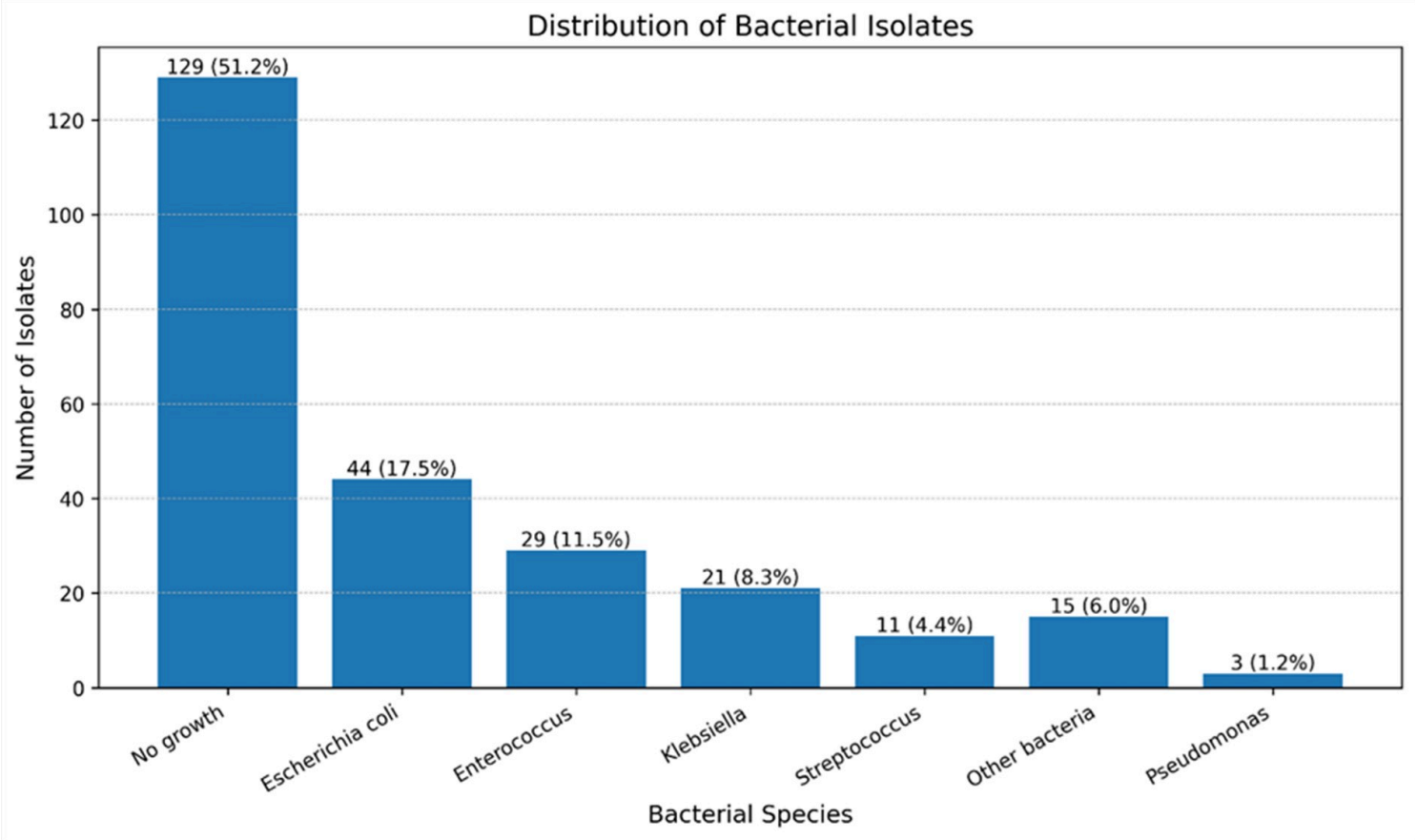


Figure 1

Grafic 1. Distribution of Bacteria Isolated from Bile Culture (N=252)

Supplementary Files

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- Table1.docx